

REACTIONS OF β -HALOSULPHONES WITH BASES AND SILVER SALTS:
THE SULPHONYL GROUP AS A WEAK ANCHIMERIC ASSISTANT

J.C. CARRETERO, J.L.GARCIA RUANO*, M.C.MARTINEZ and J.H.RODRIGUEZ

Departamento de Química. Universidad Autónoma de Madrid
Cantoblanco, 28049-Madrid, SPAIN

(Received in UK 31 July 1987)

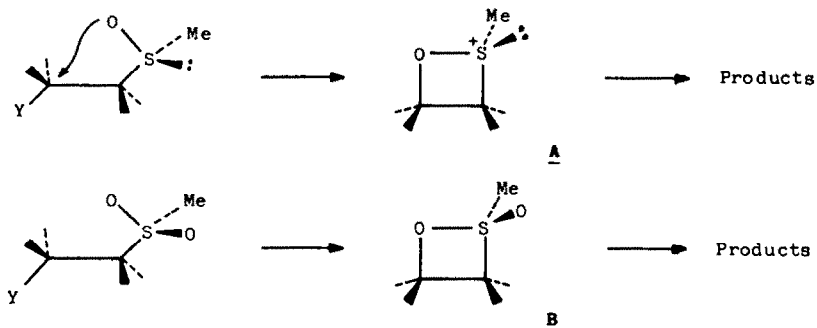
Abstract-In order to obtain evidence about the ability of the sulphone group as anchimeric assistant, the behaviour of the erythro and threo-1,2-dimethyl (and 1,2-diphenyl)-2-halo-1-methylsulphonylethanes in their reactions with $\text{NH}_4\text{OH}/\text{CH}_3\text{CN}$, NaOH/MeOH and $\text{AgBF}_4/\text{MeOH}$ is described. The participation is not detected in any case on butane derivatives or on 1,2-diphenylethane derivatives with basic nucleophiles, which yielded mainly elimination products. Reactions of the last compounds with $\text{AgBF}_4/\text{MeOH}$ only afforded mixtures of substitution products, with predominance of those with the same configuration of the starting sulphones in the case of erythro-derivatives, which must only evolve through an $\text{S}_{\text{N}}1$ mechanism in competition with the anchimeric assistant process. This is the first reported result suggesting that the weak nucleophilic character of the sulphonylic oxygens can determine its participation as anchimeric assistant in the substitution of good leaving groups in β -position.

INTRODUCTION

The studies on the reactivity of β -halothioethers with different nucleophiles have allowed the stereospecific synthesis of many β -heterosubstituted thioethers¹, taking advantage of the great ability of sulphenylic sulphur as anchimeric assistant, which controlled the course of all reactions, regardless of the nature of the nucleophile. On the contrary, the β -halosulphoxides exhibited a behaviour depending on the nucleophilic reagent. Thus, when this had a weak basic character the sulphonylic oxygen was able to act as anchimeric assistant, where the substrates evolved into the products through the cyclic alkoxysulphonium salts (A, scheme 1), whereas with more strongly basic nucleophiles the elimination products were predominant².

Sulphone oxygens show nucleophilicity only under unusual conditions. The only example known to these authors was reported by Whiting et al³ in decomposition of the arene diazonium salt in sulpholane. Thus, it is not surprising that the anchimeric assistance by the sulphone group has not been detected³, although the stabilization^{4a} or intramolecular trapping^{4b} of carbocations by this group have been suggested in brominations of some unsaturated sulphones. Taking into account the results obtained with thioethers¹ and sulphoxides², and that the β -halosulphones could evolve through intermediates like B (scheme 1) structurally similar to A, we thought that these substrates would be adequate for obtaining evidence on the participation, or not, of the sulphone group in the substitution of the halogen.

Thus, in this paper, the study of the reactions of erythro and threo-1,2-dimethyl (and 1,2-diphenyl)-2-halo-1-methylsulphonylethanes with different nucleophiles (NaOH/MeOH, NH₄OH/CH₃CN and AgBF₄/MeOH) is reported.



Scheme 1

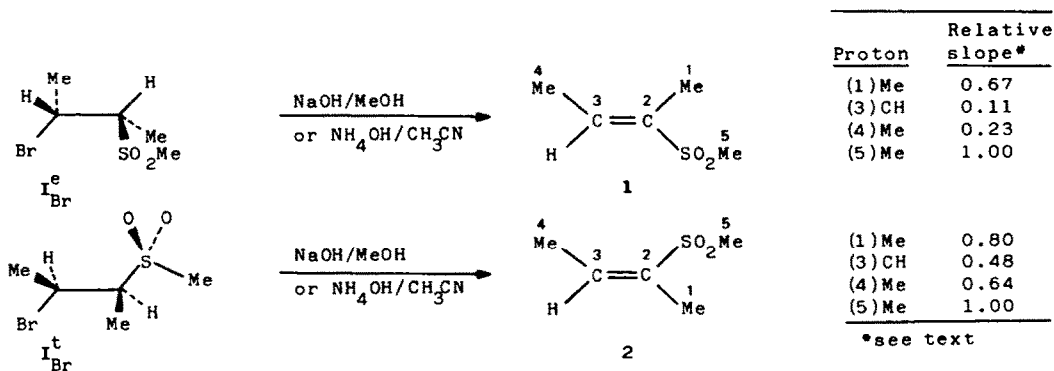
The notation used to design the halosulphones considered here is indicated in Scheme 2. Similar notation will be used in other sulphones (Y = OH, OMe, indicated as subindexes) also exhibiting butane (I) or 1,2-diphenylethane (II) skeleton. The synthesis and the conformational analysis of the sulphones in scheme 2, have been previously reported⁵.

R	Y	Configuration	
		<u>erythro</u>	<u>threo</u>
Me	Br	I _{Br} ^e	I _{Br} ^t
		II _{Cl} ^e	II _{Cl} ^t
Ph	Br	II _{Br} ^e	II _{Br} ^t

Scheme 2

RESULTS AND DISCUSSION

The reactions of I_{Br}^e and I_{Br}^t with basic nucleophiles (NaOH/MeOH and NH₄OH/CH₃CN) took place in a stereospecific way yielding, respectively, the olefins 1 and 2, whose configurations were established from their nmr-parameters (see experimental) and by study of the LIS effects⁶ using Eu(dpm)₃. The slopes obtained for the different protons, relative to that for (5) CH₃, which has been taken as 1.00 in both substrates, are indicated in scheme 3. The assignment is mainly carried out from the slopes of the protons (3)CH and (4)Me in both isomers.

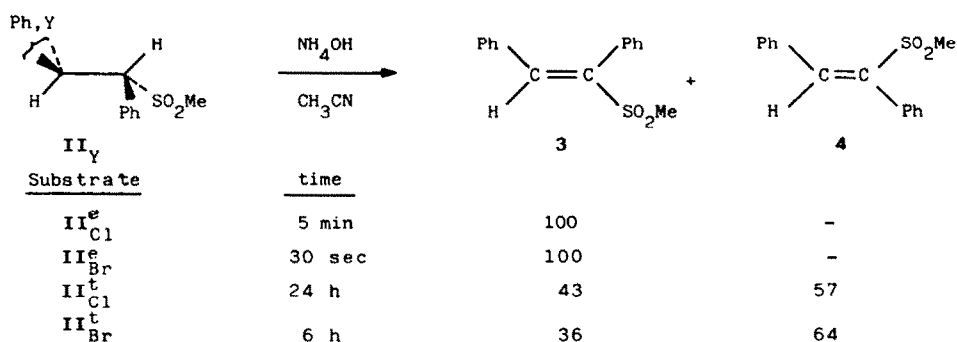


Scheme 3

The stereochemical results suggested the evolution of substrates according to an E2 mechanism. On the other hand, the higher reactivity of the erythro sulphone with respect to the threo- one⁷ can be explained from the conformational preferences of the starting materials (the rotamers depicted in scheme 3 are the favoured ones for I_{Br}^e and I_{Br}^t ⁵) taking into account the required stereochemistry for the E2 processes.

In the case of the sulphoxides with the same skeleton as that of I_Y , their reactions with $AgBF_4/MeOH$, a weaker basic nucleophile than those used before had revealed the anchimeric assistance of the sulphinylic oxygen². The reaction of I_{Br}^e with this reagent yielded only a 9:1 mixture⁸ of $1:I_{OMe}^t$ in 12 hours, while I_{Br}^t afforded, after 15 days, a 7:3 mixture of $2:I_{OMe}^e$ recovering starting material without reacting ($\sim 30\%$). The fact that the E2 and S_N2 products were the only ones detected in these reactions, indicates that the ability of the sulphone group as anchimeric assistant, if it exists, has to be much lower than that of the sulphoxide group. The higher proportion of the S_N2 product and the slower evolution observed for I_{Br}^t , must be a consequence of its aforementioned lower reactivity in E2 processes. Moreover, the stereochemistry of the favoured rotamers (scheme 3) suggests that the S_N2 processes must also be slower in I_{Br}^t than in I_{Br}^e using steric considerations.

Afterwards, we have studied the behaviour of the 2-halo-1-methylsulphonyl-1,2-diphenylethanes, II_Y^e and II_Y^t ($Y = Cl, Br$)⁵, with the same nucleophilic reagents. The benzylic character of the carbon-halogen bond, must facilitate the substitution processes on these substrates, suggesting that a weak anchimeric assistance could be more easily evidenced. Unfortunately, the reactions of II_Y^e and II_Y^t with NH_4OH/CH_3CN yielded exclusively the elimination products. The erythro sulphones evolved into (E)-1,2-diphenyl-1-methylsulphonylethylene (3) easily recognized from its nmr parameters⁹ suggesting that an E2 process has taken place. The threo-isomers yielded mixtures of the (E)- and (Z)-olefins (3 + 4), whose proportion depended on the halogen. The minimal reaction times required for the complete evolution of the substrates and the proportion of 3 and 4 in the mixtures obtained from II_Y^t (which remain constant during the process) are indicated in scheme 4.



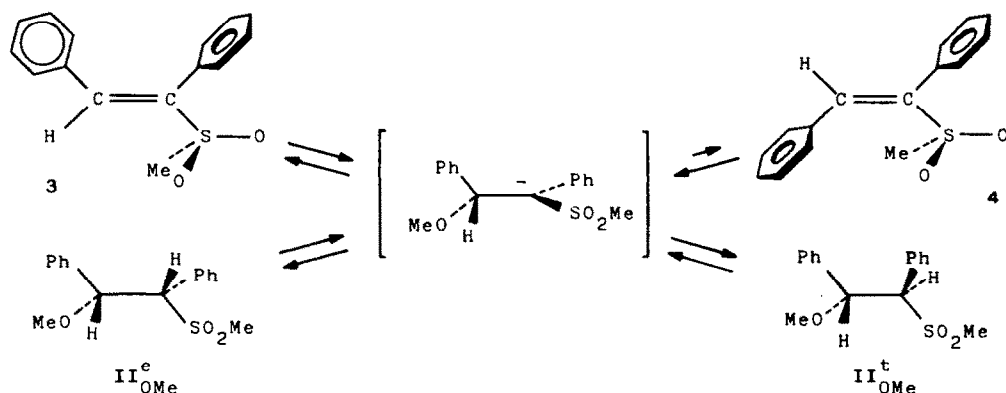
Scheme 4

The obtention of 3 from II_Y^t can only be explained assuming the formation of an α -sulphonylbenzylic carbanion evolving, at least partially, into the (E)-olefin, 3. The dependence of the composition of the 3 + 4 mixtures or the nature of the halogen indicates that the E1cB process (almost independent of the halogen) must be in competition with the E2 process (yielding 4 and being easier when $Y = Br$)¹⁰.

The large difference in the evolution rates of erythro- and threo-sulphones (see scheme 4) must be attributed to the different rate of the E2 processes on

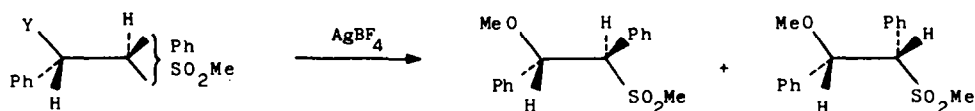
both substrates (the similar basicity of their benzylic protons does not suggest substantial changes in the E1cB rates), which can be explained on the basis of the higher stability of the olefin **3**¹¹ (see later).

The reactions of compounds II_Y ($Y = \text{Cl}, \text{Br}$) with NaOH/MeOH yielded after 10 days at room temperature a mixture of **3**, II_{OMe}^e and II_{OMe}^t , with the same proportion (60.9:7.3:31.8 respectively) in all cases. Nevertheless, when stopping the reaction at 30 seconds the starting sulphones have completely disappeared, the olefins **3** and **4** being the only existing products. As in the preceding reactions, II_Y^e yielded **3**, while from II_Y^t a mixture of **3** and **4** was formed. This indicates, that the obtained methoxysulphones are addition products on the olefin intermediates and not substitution products on II_Y . The identical final composition of the reaction mixtures, regardless of the starting sulphone indicates the state of an equilibrium between the compounds involved (scheme 5)¹². The absence of **4** in the equilibrium indicates that this must be much more unstable than **3**. The isomerization between both olefins, only observed in the sense $4 \rightarrow 3$, supports this conclusion, which is also in accordance with the isomerization experiences carried out on the (E)- and (Z)-2-phenylsulphonyl-1,2-diphenylethylene¹³. The steric interactions of the sulphone group with the aromatic rings in olefins **3** and **4**, suggest that the favoured stereochemistry in each is that depicted in scheme 5. As we can see, the larger conjugation (and therefore larger stability) corresponds to (E)-olefin **3**. This explanation is in accordance with the λ_{max} and ϵ values assigned to both isomers in compounds of similar structure¹³.



The reactions of II_Y ($Y = \text{Cl}, \text{Br}$) with $\text{AgBF}_4/\text{MeOH}$ afforded mixtures of β -methoxysulphones (see proportions in scheme 6). The low basic character of the methanol justifies the absence of the elimination products, while its weak nucleophilicity excludes the possibility that the obtained substitution products could come from the nucleophilic addition to the double bond¹⁴ (in that case olefin **3** would probable be detected among the reaction products).

The threo-halosulphones yielded mixtures in which erythro-methoxysulphones are predominant. The competition between $\text{S}_{\text{N}}2$ (yielding II_{OMe}^e with inversion in the configuration) and $\text{S}_{\text{N}}1$ processes (causing racemization and therefore a mixture of II_{OMe}^e and II_{OMe}^t) satisfactorily explain the obtained results. The decrease of the methanol concentration, diminishes the proportion of molecules evolving through the $\text{S}_{\text{N}}2$ mechanism, and so, the treatment of II_{Br}^t with AgBF_4 in CHCl_3 containing 5% of methanol, gave an equimolecular mixture of both methoxysulphones, which indicate the complete transformation of the substrate by the $\text{S}_{\text{N}}1$ mechanism.

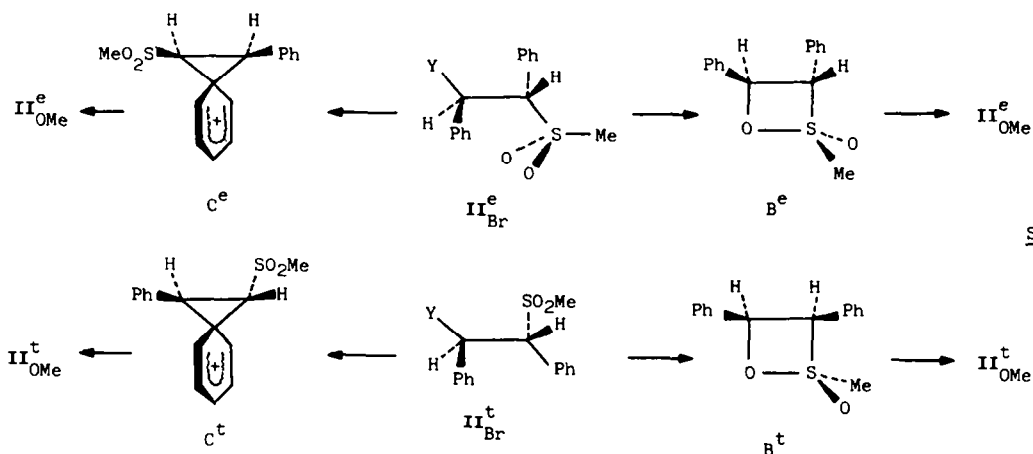


Substrate	Solvent*	II _{OMe} ^e	II _{OMe} ^t
II _{Cl} ^e	A (B)	63(70)	37(30)
II _{Br} ^e	A (B)	58(63)	42 (37)
II _{Cl} ^t	A	72	28
II _{Br} ^t	A (B)	74(50)	26 (50)

* A = MeOH, B = CHCl₃+5% MeOH

Scheme 6

The erythro-halosulphones yielded mixtures (see Scheme 6), in which the major II_{OMe}^e, also exhibited the erythro- configuration. This result can only be rationalized by assuming that the anchimeric assistance of the SO₂Me or Ph group, to the leaving halogen, determining retention in the configuration takes place to some extent. The participation of the phenyl group, which would generate the C intermediates (scheme 7), can be reasonably excluded. From a steric point of view, C^t must be much more stable than C^e. Moreover, the formation of C^t must be easier than that of C^e because the favoured rotamer for their respective starting materials (depicted in scheme 7) exhibits the adequate stereochemistry for the participation of the phenyl group in the case of II_{Br}^t, but not in that of II_{Br}^e. Therefore, if the phenyl group acted as anchimeric assistant, its effect would have to be more significant on the substrate exhibiting threo- configuration¹⁵, which is in opposition to the experimental results.



Scheme 7

On the contrary, the higher stability of B^e and its easier formation from its starting sulphone (both with respect to B^t)¹⁶ whose favoured rotamer exhibit the adequate stereochemistry for the SO₂Me participation, satisfactorily explain that the anchimeric assistance competes, only in the case of erythro sulphones, with other processes determining inversion of configuration or racemization.

The experiments performed on II_Y^e, decreasing the concentration of the nucleophile (by using CHCl₃ and 5% MeOH as solvent), indicate that only a slight increase in the percentage of II_{OMe}^e is produced (see scheme 7). This suggests that the S_N2 mechanism has little significance as an evolution pathway of the erythro sulphones, which must therefore evolve through an S_N1 process in competition with the anchimeric assistance process. Taking into account that as concentration of MeOH decreases the medium polarity also diminishes, which favours

the anchimeric assistance process with respect to the S_N1 process, it is possible to explain the observed changes in the composition of the reaction mixtures when the concentration of MeOH is modified.

As can be easily deduced from scheme 7, the steric and electronic interactions between the SO_2Me group and the nucleophile in its approach to II_Y^e , according to a S_N2 process, must be larger than those between the phenyl group and the nucleophile in the case of II_Y^t . This justifies the different ability of both substrates to evolve through a S_N2 mechanism.

As we can see (scheme 7) only 40% of the molecules evolved with participation of the sulphone group in the most favourable case, with preference to the alternative S_N1 mechanism. Thus, we can conclude that the weak nucleophilic character of the sulphonylic oxygens only permits the SO_2Me group of β -halosulphones to act as anchimeric assistant under very favourable conditions, in which the substrates cannot evolve by other competitive pathways.

EXPERIMENTAL

The nmr spectra of all samples were recorded as $CDCl_3$ solutions on a Bruker WP-200-SY spectrometer in TF mode. The synthesis of β -halosulphones used in this work as starting materials has been previously described⁵. The reaction times were indicated in the previous section and the composition of the crude reaction mixtures was determined by 1H -nmr using the intensities of the well separated signals.

Reaction of β -halosulphones. a) With sodium hydroxide: 1 mmol of the corresponding β -halosulphone was solved in 30 ml of a 1% aqueous-methanolic solution (1:1) of sodium hydroxide. The reaction mixture was allowed to stand at room temperature and extracted with methylene chloride. The combined extracts were washed with water, dried over anhydrous sodium sulphate and the solvent was removed under reduced pressure. B) With ammonium hydroxide: To a solution of 1 mmol of the β -halosulphone in 10 ml of acetonitrile were added 10 ml of 20% ammonium hydroxide. The reaction mixture was diluted with 20 ml of water and the isolation of the reaction products were carried out as described in A. C) With silver tetrafluoroborate: A 0.19 g (1 mmol) sample of silver tetrafluoroborate was added to a well stirred solution of 1 mmol of the β -halosulphone in 20 ml of methanol (or chloroform containing 5% of methanol). The reaction mixture was worked up as described in A.

Compounds 1 and 2 were obtained as viscous liquids from I_{Br}^t and I_{Br}^t respectively and purified by column chromatography (silica gel Merck K-60, 70-230 mesh and CH_2Cl_2 as eluent); found 1, C 45.01; H 7.38, S 24.00, 2, C 44.93; H, 7.50,

Table 1. Spectroscopic data of compounds 1 and 2

	1H -nmr ^a				^{13}C -nmr ^a							
	Chemical shifts (ppm)				Chemical shifts (ppm)							
	H(1)	H(3)	H(4)	H(5)	J_{13}	J_{34}	J_{14}	C(1)	C(2)	C(3)	C(4)	C(5)
1	2.05	6.83	1.86	2.86	1.4	7.0	1.2	11.3	137.5	136.4	13.8	40.2
2	2.09	6.24	2.11	2.92	1.5	7.4	1.6	19.9	137.0	137.6	14.6	41.9
	IR (film)				ν_{max}^b			UV λ_{max}^{EtOH} (ϵ) ^c				
1	1655, 1293, 1170, 1117,				963, 762, 676, 669, 536, 523			205 (4250)				
2	1650, 1296, 1176, 1123,				959, 838, 759, 610, 543			205 (8000)				
	MS m/z (intensity) ^d											
1	134 (M^+)(18.8), 119 (1.3), 91 (26.7), 81 (18.7), 72 (8.3), 71 (56.6), 64 (12.0), 63 (11.1), 55 (100), 53 (29.0), 43 (34.1)											
2	134 (M^+)(100), 119 (0.5), 91 (16.0), 81 (48.0), 72 (6.7), 71 (26.9), 65 (6.9), 63 (20.9), 55 (96.5), 53 (33.7), 43 (31.4)											

^a From internal TMS. Numbering is shown in scheme 3. ^b Recorded on a Nicolet DX spectrophotometer. ^c Recorded on a Perkin Elmer 124 spectrophotometer. ^d Recorded on a HP-5985 spectrometer at 70 eV.

S 24.30. 1 and 2 require C 44.75, H 7.51, S 23.89. Spectral parameters are shown in table 1. Assignment of the different resonances to each individual proton was done on the basis of proton-proton coupling constants and chemical shift changes in the presence of $Eu(dpm)_3$. ^{13}C -nmr assignment of the methyl groups was performed by bidimensional 1H - ^{13}C nmr correlated spectroscopy.

REFERENCES AND NOTES

1. J.C. Carretero, J.L. García Ruano, M.C. Martínez and J.H. Rodríguez, **J.Chem. Research (S)** 1985, 5 (M) 172.
2. J.C. Carretero, J.L. García Ruano and J.H. Rodríguez, XII International Symposium on the Organic Chemistry of Sulphur, Nijmegen (The Netherland) July, Abstracts OB8.
3. G.R. Chalkley, D.J. Snodin, G.Stevens and M.C. Whiting, **J.Chem.Soc.(C)**, 1970, 682.
4. a) J.I.G. Cadogan, D.K. Cameron, I. Gosney, R.M. Highcock and S.F. Newlands, **J.Chem.Soc., Chem.Commun.**, 1985, 1751. b) S. Braverman and D. Reisman, **Tetrahedron Letters**, 1977, 1756.
5. J.C. Carretero, J.L. García Ruano, M.C. Martínez, J.H. Rodríguez, **An.Quim.**, 1987, (in the press).
6. R. Von Ammon and R.D. Fischer, **Angew.Chem.Internat. Ed.**, 11, 675 (1972).
7. The following of the reactions with $\text{NH}_4\text{OH}/\text{CD}_3\text{CN}$ in the sample tube of the nmr spectrometer indicated that $\text{I}_{\text{Br}}^{\text{t}}$ required 30 minutes for its total evolution, whereas $\text{I}_{\text{Br}}^{\text{e}}$ disappeared completely in 1 minute. The reactions of both substrates with $\text{NaOH}/\text{CD}_3\text{OD}$ are instantaneous.
8. The configuration and spectroscopic parameters of the β -methoxysulphones $\text{I}_{\text{OMe}}^{\text{e}}$ and $\text{I}_{\text{OMe}}^{\text{t}}$ as well as $\text{II}_{\text{OMe}}^{\text{e}}$ and $\text{II}_{\text{OMe}}^{\text{t}}$ were known (J.C.Carretero, J.L.García Ruano, M.C. Martínez, J.H. Rodríguez and F.Alcudia, **Tetrahedron**, 41, 2419 (1985).
9. F.Bonini, G. Maccagnani, G. Mazzanti and P. Piccinelli, **Tetrahedron Letters**, 41, 3987 (1979).
10. Taking into account that higher base concentrations favoured the E_{icB} processes with respect to the E_2 one (J.March in *Advanced Organic Chemistry*, John Wiley and Sons, New York, 1985, p. 895) we have carried out several trials, varying the proportion of the NH_4OH (but always great excess with respect to the substrate $\text{II}_{\text{Br}}^{\text{t}}$). The results indicated that, both the total rate and the proportion of **3** in the mixture, were greater as the concentration of the base increased.
11. Conformational factors cannot be invoked to justify these differences, because the favoured rotamers in all sulphones II_Y ($Y = \text{Cl}, \text{Br}$) exhibited an anti-periplanar arrangement between the hydrogens⁵ as indicated in scheme 4.
12. The reactions of **1** and **2** with NaOH/MeOH have also been studied. These processes which require much longer reaction times than those for **3** and **4** (5 or 6 months at room temperature), are not reversible, yielding the corresponding methoxy-sulphones $\text{I}_{\text{OMe}}^{\text{e}}$ and $\text{I}_{\text{OMe}}^{\text{t}}$. The isomerization $2 \rightarrow 1$ (but not $1 \rightarrow 2$) can also be observed.
13. B.B. Jarvis, W.P. Tong and H.L. Ammon, **J.Org.Chem.**, 40, 3189 (1975).
14. When **3** was treated with MeOH over a long period, it was recovered unchanged.
15. This behaviour has been observed in the halogen exchange reaction on erythro- and threo-1,2-diphenyl-1-propylchloride. See D.J. Cram and F.A. Abd Elhafez, **J.Am.Chem.Soc.**, 74, 5851 (1952).
16. Although two different structures (epimers at sulphur) should be considered for B^{e} and B^{t} , in scheme 7 we have only represented the presumably more stable ones, from a steric point of view.